

CLAIMS

What is claimed is:

- 1 1. A method of therapy for a mammal at risk of, or afflicted with, loss of or damage to  
2 myocardium, the method comprising  
3       implanting a preparation of myogenic precursor cells into said mammal at a site at risk of,  
4 or afflicted with, loss of or damage to myocardium, and  
5       treating said myogenic precursor cells with an amount of a morphogen sufficient to  
6 promote proliferation or differentiation of said myogenic precursor cells into functional  
7 myocardium.
- 1 2. A method of therapy for a mammal at risk of, or afflicted with, loss of or damage to  
2 myocardium, the method comprising  
3       implanting a preparation of myogenic precursor cells into said mammal at a site at risk of,  
4 or afflicted with, loss of or damage to myocardium, and  
5       treating said mammal with an amount of an inducer of a morphogen encoded by a gene of  
6 said mammal, said amount being sufficient to promote proliferation or differentiation of said  
7 myogenic precursor cells into functional myocardium.
- 1 3. A method of therapy for a mammal at risk of, or afflicted with, loss of or damage to  
2 myocardium, the method comprising  
3       implanting a preparation of myogenic precursor cells into said mammal at a site at risk of,  
4 or afflicted with, loss of or damage to myocardium, and  
5       treating said myogenic precursor cells with an amount of an agonist of a morphogen  
6 receptor expressed by said myogenic precursor cells, said amount being sufficient to promote  
7 proliferation or differentiation of said myogenic precursor cells into functional myocardium.
- 1 4. A method of therapy for a mammal at risk of, or afflicted with, loss of or damage to  
2 myocardium, the method comprising  
3       implanting a preparation of myogenic precursor cells into said mammal at a site at risk of,  
4 or afflicted with, loss of or damage to myocardium, and

5       treating said myogenic precursor cells with an amount of a small molecule morphogenic  
6       activator, said amount being sufficient to promote proliferation or differentiation of said myogenic  
7       precursor cells into functional myocardium.

1       5.       A method as in any one of claims 1-4 wherein said myogenic precursor cells are selected  
2       from the group consisting of mammalian skeletal muscle satellite cells, embryonic myogenic  
3       precursor cells, and a histocompatible mammalian myogenic precursor cell line.

1       6.       A method as in any one of claims 1-4 wherein said myogenic precursor cells are  
2       autologous skeletal muscle satellite cells.

1       7.       A method as in any one of claims 1-4 wherein  
2       said mammal is afflicted with a condition selected from the group consisting of myocardial  
3       infarction and congestive heart failure.

1       8.       A method as in any one of claims 1-4 wherein said treatment step is conducted prior to  
2       said implantation step.

1       9.       A method as in any one of claims 1-4 wherein said treatment step is conducted  
2       simultaneous with said implantation step.

1       10.      A method as in any one of claims 1-4 wherein said treatment step is conducted subsequent  
2       to said implantation step.

1       11.      A method as in claim 10 wherein said treatment step is at least once a week for a period of  
2       at least four weeks.

1       12.      A method as in claim 10 wherein said treatment step is at least once a month for a period  
2       of at least one year.

1       13.      A method as in claim 1 wherein said morphogen treatment step is conducted with  
2       morphogen at a concentration of about 0.01-1000 ng/ml.

1       14.      A method as in claim 1 wherein said morphogen treatment step is conducted with  
2       morphogen at a concentration of about 0.1-100 ng/ml.

1       15.      A method of promoting proliferation of myogenic precursor cells or differentiation of  
2       myogenic precursor cells into functional myocardium comprising the steps of.

3 (a) contacting said cells with a morphogen in an amount effective to induce said  
4 proliferation or differentiation; and

5 (b) maintaining said cells in a morphogenically permissive environment.

1 16. A method as in claim 1 wherein said morphogen is selected from the group consisting of a  
2 pro form of a morphogen, a soluble form of a morphogen, a mature morphogen, and a C-terminal  
3 fragment of a morphogen comprising at least the seven cysteine domain of said morphogen.

1 17. A method as in claim 1 wherein said morphogen is selected from the group consisting of  
2 osteogenic proteins and bone morphogenic proteins.

1 18. A method as in claim 1 wherein said morphogen  
2 induces a cascade of tissue-specific morphogenesis culminating in the formation of  
3 functional mammalian myocardium; and  
4 comprises a pair of folded polypeptides, the amino acid sequence of each of which  
5 comprises a sequence having at least 70% amino acid sequence homology with the C-terminal  
6 seven-cysteine domain of human OP-1, mouse OP-1, human OP-2 or mouse OP-2, residues 38-  
7 139 of SEQ ID NOs. 5, 6, 7 or 8, respectively.

1 19. A method as in claim 1 wherein said morphogen is selected from the group consisting of  
2 OP-1, CBMP-2A (BMP-2), and CBMP-2B (BMP-4).

1 20. A therapeutic composition for promoting the repair or regeneration of mammalian  
2 myocardium comprising  
3 isolated mammalian myogenic precursor cells, and  
4 an amount of a morphogen sufficient to promote proliferation or differentiation of said  
5 myogenic precursor cells into functional myocardium in a morphogenically permissive  
6 environment.

1 21. A therapeutic composition for promoting the repair or regeneration of mammalian  
2 myocardium comprising  
3 isolated mammalian myogenic precursor cells, and

4 an amount of an inducer of a morphogen sufficient to promote proliferation or  
5 differentiation of said myogenic precursor cells into functional myocardium in a morphogenically  
6 permissive environment.

1 22. A therapeutic composition for promoting the repair or regeneration of mammalian  
2 myocardium comprising

3 isolated mammalian myogenic precursor cells, and

4 an amount of an agonist of a morphogen receptor sufficient to promote proliferation or  
5 differentiation of said myogenic precursor cells into functional myocardium in a morphogenically  
6 permissive environment.

1 23. A therapeutic composition for promoting the repair or regeneration of mammalian  
2 myocardium comprising

3 isolated mammalian myogenic precursor cells, and

4 an amount of a small molecule morphogenic activator sufficient to promote proliferation  
5 or differentiation of said myogenic precursor cells into functional myocardium in a  
6 morphogenically permissive environment.

1 24. A method of culturing mammalian myogenic precursor cells comprising  
2 isolating said myogenic precursor cells, and  
3 culturing said myogenic precursor cells in a medium comprising an amount of a  
4 morphogen sufficient to promote proliferation or differentiation of said myogenic precursor cells  
5 into functional myocardium in a morphogenically permissive environment.

1 25. A method of culturing mammalian myogenic precursor cells comprising  
2 isolating said myogenic precursor cells, and  
3 culturing said myogenic precursor cells in a medium comprising an amount of an inducer  
4 of a morphogen sufficient to promote proliferation or differentiation of said myogenic precursor  
5 cells into functional myocardium in a morphogenically permissive environment.

1 26. A method of culturing mammalian myogenic precursor cells comprising  
2 isolating said myogenic precursor cells, and

3 culturing said myogenic precursor cells in a medium comprising an amount of an agonist  
4 of a morphogen receptor sufficient to promote proliferation or differentiation of said myogenic  
5 precursor cells into functional myocardium in a morphogenically permissive environment.

1 27. A method of culturing mammalian myogenic precursor cells comprising  
2 isolating said myogenic precursor cells, and  
3 culturing said myogenic precursor cells in a medium comprising an amount of a small  
4 molecule morphogenic activator sufficient to promote proliferation or differentiation of said  
5 myogenic precursor cells into functional myocardium in a morphogenically permissive  
6 environment.

1 28. A method of inducing myogenic precursor cells, naturally competent to differentiate into  
2 skeletal or smooth muscle, to differentiate into cardiomyocytes, said method comprising the steps  
3 of  
4 (a) contacting said myogenic precursor cells with a morphogen; and  
5 (b) maintaining the product of (a) in an environment morphogenically permissive for  
6 cardiomyogenesis.

1 29. A method of producing replacement cardiomyocytes in a mammal in need thereof, said  
2 method comprising the step of implanting into said mammal myogenic precursor cells induced by  
3 the method of claim 28.

1 30. A pharmaceutical composition comprising  
2 a morphogenic agent selected from the group consisting of a morphogen, a morphogen  
3 inducer, an agonist of a morphogen receptor, and a small molecule morphogenic activator; and  
4 a mitogen selected from the group consisting of bFGF, IGF, PDGF, LIF, ACTH, MSH,  
5 and G-CSF.